REMARKS

These remarks are in response to the Office Action mailed November 16, 2004. Claims 1 and 17-19 have been amended. Support for the amendments can be found throughout the specification. Claims 1-13 and 15-32 are presently pending. Claim 14 was previously canceled. No new matter has been added and entry of the amendment is respectfully requested.

Claims 1 and 17-19 have been amended to clearly recite a composition claim (e.g. "cell culture comprising" or an "EBD cell culture comprising") and *not* a composition claim which can be interpreted as a product by process claim.

The Office Action states that, before amendment, the claims are product by process claims: a cell culture derived from human embryoid body cells (page 2 of Office Action). Because, according to the Office Action, the claims are product by process claims, a cell expressing *any* one marker that is found in ectodermal, mesodermal or endodermal cell falls within the scope of the claim, and thereby anticipates the claimed invention.

Applicants note that the originally filed claims, 1 and 17-19, and dependent claims therein are compositions claims and not product by process claims. Amendment of the claims does not add new subject matter nor does it raise new issues.

II. Rejection Under 35 U.S.C. §102(b)

The following sets of claims are rejected under 35 USC §102(b), as allegedly being anticipated because it was patented or described in a printed publication in this or a foreign country. Applicants respectfully traverse these rejections.

Under 35 USC § 102, "[a] claim is anticipated only if *each and every element* as set forth in the claim is found, either expressly or inherently described, in a single prior art reference (emphasis added)." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 0987). Further , "[t]he identical invention [should it be taught in the cited reference] must be shown in as complete detail as is contained in the ...claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Applicants submit that in view of the following remarks, and after amendment of the claims, none of the cited references anticipates the claimed invention, because each reference does not teach *each and every element* of the claimed invention.

Further, Applicants request clarification of many of the rejections made under 35 USC §102 below, because the rejections do not clearly or accurately state where in the body of the text of the cited references the Office Action is drawing the substantive data to reject the claims, and because the rejections are based on an interpreting the claims as product by process claims. However, Applicants have made a detail review of all cited references. Although a few of the references do not contain the teachings that are stated in the Office Action, to be complete, the remarks below are fully responsive to each and every rejection made under 35 USC §102.

A. Claims 1-5, 9-13, 15, 16 and 18-20 are rejected under 35 USC §102(b), as allegedly being anticipated by Allsopp et al. (hereinafter, "Allsopp"). Applicants traverse this rejection.

The Office Action states that Allsopp describes the following: (1) human clonal fibroblast cells; (2) cells do not form teratomas when injected in SCID mice; (3) cells that express nestin mRNA and another marker from ectodermal, mesodermal or endodermal cells; (4) 30-60 population doublings; (5) cells that proliferate under conditions that are nonpermissive for proliferation of human embryonic germ cells; (6) cells that proliferate in media lacking LIF and/or fibroblast feeder layer; and (7) cells that are transfectable with retrovirus and lentovirus.

After detailed review of Allsopp, Applicants submit that all the teachings (1) – (7) above are not taught by Allsopp as the Office Action has stated. Allsopp discusses the variability in telemore length among clonal fibroblast populations at early passage and at senescence (page 132, col. 2, first paragraph under the Discussion). Hence, while Allsopp may show human clonal fibroblast cells (1), Allsopp does not teach (2) – (7). For example, no where in Allsopp is there mention of fibroblasts not forming teratomas when injected in SCID mice (2); or of fibroblasts expressing nestin mRNA and another marker from ectodermal, mesodermal or endodermal cells (3); or clonal fibroblasts undergoing 30-60 population doublings (4); or of fibroblasts proliferating under conditions that are nonpermissive for proliferation of human embryonic germ cells (5); or fibroblasts proliferating in media lacking LIF and/or fibroblast feeder layer (6); or of fibroblasts being transfectable with retrovirus and lentovirus (7).

Further, even after amendment of the claims, Allsopp still does not anticipate the claimed invention because Allsopp does not teach a cell culture from EBD cells, which do not cause teratoma formation in SCID mice and that simultaneously express a polypeptide or mRNA from at least two types of cells selected from ectodermal, mesodermal or endodermal cell. In fact, Allsopp describes an end product which is not derived from an embryoid body.

Accordingly, withdrawal of the rejection of claims 1-5, 9-13, 15, 16 and 18-20 under 35 USC §102 is respectfully requested.

B. Claims 1-6 and 8 are rejected under 35 USC §102(b), as allegedly being anticipated by Jin et al (1993). Applicants respectfully traverse this rejection.

According to the Office Action, Jin teaches clonal myoblasts expressing myf6 and inherently expressing nestin and that this meets the limitation that cells express polypeptide or mRNA markers characteristic of two different cell types (ectodermal, mesodermal, and/or endodermal).

However, Jin does not teach myoblast expressing myf6 and nestin from embryoid body derived cells and cells which do not cause teratomas in SCID mice. The pending claims recite cells which are embryoid body derived cells that do not cause teratomas in SCID mice and express at least a polypeptide or mRNA markers from two different cell types. Therefore, since each and every element of the claimed invention is not taught in Jin, Jin cannot anticipate the claimed invention.

Accordingly, withdrawal of the rejection of claims 1-6 and 8 under 35 USC §102 is respectfully requested.

C. Claims 1-7 are rejected under 35 USC §102(b), as allegedly being anticipated by Suzuki et al (1996). Applicants respectfully traverse this rejection.

According to the Office Action, Suzuki teaches differentiating myocytes expressing GATA-4, and gastrointestinal tissues composed of at least two different types of cells. However, upon detailed review of Suzuki, Applicants submit that Suzuki teaches differentiating myocytes derived from vascular smooth muscle cells (VSMCs) expressing GATA-6, *not* GATA-4 as stated in the Office Action (see Suzuki Abstract; page 284, col. 1, first complete paragraph before Materials and Methods; page 285, col. 2, paragraph under "Regulated GATA-6 Expression in VSMCs;" and throughout the discussion starting on page 287). In fact, Suzuki describes that "GATA-4 expression is *not* detected in human or rat VSMCs" (see page 285, col. 2, last sentence in the paragraph under "Regulated GATA-6 Expression in VSMCs"). Hence, Suzuki does *not* teach the claimed invention, in particular claims 1 and 7.

Also, after a detailed review of Suzuki, Applicants submit that there is no mention of "gastrointestinal tissues composed of mesodermal and endodermal cells," as alleged by the Office Action (see page 3). Further, even if Suzuki did teach "gastrointestinal tissues composed of mesodermal and endodermal cells," Suzuki would also have to teach that they express at least a polypeptide or mRNA marker from mesodermal or endodermal cells. That is, in order to anticipate the claimed invention, the myocytes alone have to express at least a polypeptide or mRNA marker from two different types of cells; and/or the gastrointestinal tissue alone has to show at least a polypeptide or mRNA marker from two different types of cells. However, Suzuki neither teaches myocytes expressing GATA-6 and no other marker or polypeptide from another type of cell, nor does Suzuki teach any gastrointestinal tissue, let alone any gastrointestinal tissue expressing a polypeptide or mRNA marker in two different types of cells. Therefore, since each and every element of the claimed invention is not taught in Suzuki, Suzuki does not anticipate the claimed invention.

Accordingly, withdrawal of the rejection of claims 1-7 under 35 USC §102 is respectfully requested.

D. Claims 17, 19 and 21 are rejected under 35 USC §102(b), as allegedly being anticipated by Damjanov et al (1993). Applicants respectfully traverse this rejection.

According to the Office Action, Damjanov describes a tumor derived cell line, which express both vimentin and alpha-fetoprotein and upon transformation are capable of proliferating for at least 30 population doublings. Damjanov does not teach an embryoid body derived cell which can proliferate for at least 30 population doublings (claim 17), proliferating in LIF, a fibroblast feeder layer, or both, and transfectable with a retro or lentivirus or both and which do no cause teratomas when injected in SCID mice (claim 19). Therefore, since each and every element of the claimed invention is not taught in Damjanov, Damjanov does not anticipate the claimed invention.

Accordingly, withdrawal of the rejection of claims 17, 19 and 21 under 35 USC §102 is respectfully requested.

E. Claims 1, 11-13 and 15-19 are rejected under 35 USC §102(b), as allegedly being anticipated by Lefebvre et al (1998). Applicants respectfully traverse this rejection.

According to the Office Action, Lefebvre describes pancreatic islet cells with markers *not* characteristic of any two ectodermal, endodermal or mesodermal cells (see page 4). Applicants request that the Office Action clarify this rejection because the claims, recite "wherein at least some of the cells simultaneously express polypeptide or mRNA markers that are characteristic of at least two different cell types, wherein the cell types are selected from ectodermal cells, mesodermal cells, or endodermal cells." That is, the subject matter of the claimed invention claims those cells which *do* express markers (i.e. polypeptide or mRNA) from at least two of the three different cells types, and not those cells that do not. Therefore, since each and every element of the claimed invention is not taught in Lefebvre, Lefebvre does not anticipate the claimed invention.

Accordingly, withdrawal of the rejection of claims 1, 11-13 and 15-19 under 35 USC §102 is respectfully requested.

III. Rejections Under 35 U.S.C. §103(a)

Claims 21-32 are rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Shamblott et al (1998) in view of Yuen et al (1998). Applicants traverse the rejection.

The rejection appears to be based on the methods of claims 22-32. Applicants note that claim 21 is dependent on claim 19, a composition claim, and the rejection to claim 19 will not be addressed here as it was addressed above.

Claim 22 has been amended to include recitation of "in serum, reduced serum or serum-free media" to method step (b), and is fully supported by the specification in Examples 3 and 10 (page 46, paragraph 134; and page 67, paragraph 182). The specification states that regulating the level of serum in the media helps "to define and control the growth processes and avoid uncontrolled effects of serum components...[including] variable variety of growth factors known to be present in serum (Example 3, page 46, paragraph 134)."

According to the Office Action, Shamblott in view of Yuen teach all the claim limitations. Applicants argue that Shamblott in view of Yuen do not teach all the claim limitations. Shamblott teaches human pluripotent stem cells that differentiate *in vivo* into ectodermal, endodermal, and mesodermal derivatives, and are capable forming embryoid bodies (page 13729, 4th paragraph under the "Discussion"). However, Shamblott does not teach disassociation of the cells to provide a constituent cell, nor does Shamblott teach that embryoid body derived cells can be maintained in reduced serum or serum free media. Cells in Shamblott are grown in DMEM supplemented with 15% fetal bovine serum (page 13727, col. 1, line 3).

Then, according to the Office Action, Yuen teaches what is not taught in Shamblott, by teaching disaggregation or disassociation of cells in media. Similar to Shamblott, Yuen does not teach that embryoid body derived cells can be maintained in reduced serum or serum free media. After dissociation, embryoid body cells in Yuen are grown in DMEM supplemented with 15% plasma derived serum (page 3203, col. 1, line 9) and are further maintained in 10% FCS (page 3203, col. 1, line 17).

Therefore, neither Shamblott alone nor in combination with Yuen provide methods of making an embryoid body derived cell culture in media containing serum, reduced serum or serum free, and cells which express a polypeptide or mRNA from at least two different cell types (see amended claim 22), nor do they render such methods obvious.

Accordingly, withdrawal of the rejection of claims 22-32 under 35 USC §103 respectfully requested.

IV. Conclusion

Applicants submit that the pending claims are in condition for allowance. Reexamination, reconsideration, withdrawal of the rejections, and early indication of allowance are requested respectfully. If any questions remain, the Examiner is urged to contact the undersigned below.

No fee is believed due in connection with this Amendment. If any additional fees are due, the Commissioner is hereby authorized to charge any fees that may be required by this paper to Deposit Account No. 07-1896. A duplicate copy of this Transmittal Sheet is attached.

Respectfully submitted,

Date: February 7, 2004

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